Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
R 03106		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/FR2004/001790	08.07.2004	16.07.2003
International Patent Classification (IPC) or national classification and IPC		
C01B25/32, A61K9/20		
Applicant		
RHODIA CHIMIE		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FR2004/001790

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-21 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1-33 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets 1/6-6/6 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FR2004/001790

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	13, 17-21, 28-33	YES
	Claims	1-12, 14-16, 22-27	NO
Inventive step (IS)	Claims		YES
	Claims	1-33	NO
Industrial applicability (IA)	Claims	1-33	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

D1: PONTIER C ET AL: "About the use of stoichiometric hydroxyapatite in compression - incidence of manufacturing process on compressibility" EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 51, no. 3, May 2001 (2001-05), pages 249-257, XP004239486 ISSN: 0939-6411;

D2: ITOH, HIDEAKI ET AL: "A new porous hydroxyapatite ceramic prepared by cold isostatic pressing and sintering synthesized flaky powder" DENTAL MATERIALS JOURNAL (1994), 13(1), 25-35, 1994, XP008027708;

D3: WO 02/089775 A (ETHYPHARM; CHENEVIER, PHILIPPE) 14 November 2002 (2002-11-14).

1 - Clarity:

In claims 6 and 8, the use of the term "good" to characterise flow and compressibility properties,

respectively, does not enable the subject matter of said claims to be unambiguously delimited in relation to the prior art (PCT Article 6).

2 - **Novelty:**

D1 discloses a study on the influence of the various parameters of a stoichiometric hydroxyapatite on its compressibility (calcining, dry or wet granulation and granule size) with a view to its use as a carrier in tablets produced by means of direct compression.

The study was carried out on two categories of mean granule sizes, namely 200 microns and 400 microns. Moreover, D1 specifies that the mean size of 200 microns is the one most commonly used in direct compression (see D1, page 250, table 1 and paragraph 1, right-hand column).

In figure 4 on page 253, the particle size distribution curves are illustrated by a solid line and a broken line for the "200 micron" and "400 micron" batches, respectively.

The solid line demonstrates that 90% of the particles are smaller than 300 microns and that more than 90% of said particles are larger than 10 microns.

Moreover, the median diameter D50 is 185 to 225 microns (D1, page 253, right-hand column,

paragraph 1).

The specific surface area of the "200 micron" batches is 10 to 100 m^2/g (see D1, page 253, table 2).

It follows that the subject matter of claims 1, 2, 5, 6, 8, 11, 24, 25, 26 and 27 is not novel over D1 (PCT Article 33(2)).

D2 discloses a method for preparing hydroxyapatite (HAp) from brushite by means of two-step hydrolytic conversion and using a basic solution (for example, NH4OH). The first step in this method produces a non-stoichiometric HAp and the second step produces the stoichiometric material. This method is based on the conventional single-step method and is intended to enhance productivity (D2, page 4247, right-hand column).

Figure 6-A1 on page 4250 shows the brushite that is used. In view of the scale provided, it appears that the particle size of this material complies with the conditions disclosed in the subject matter of claim 12.

The reaction pH can be adjusted using NH4OH.

What is more, the reaction pH is between 7 and 8.5 for the conversion into HAp and the temperature is between 40 and 80°C (D2, page 4248, left-hand

column).

Figure 2 on page 4248 shows that, in step 1 of the method and for a pH of 9 and a temperature of 80°C, it is possible to produce HAp that has a Ca/P ratio tending towards 1.6.

The material produced in step 1 is filtered, washed and dried at 80°C (D2, page 4247, right-hand column).

As a result, the subject matter of claims 1-12, 14-16 and 22-24 is not novel over D2 (PCT Article 33(2)).

3 - Inventive step

3.1 Claims 13 and 17-21:

The technical features disclosed in claims 17 to 21 are all alternatives based on the method disclosed in D2 and would constitute a routine technical step for a person skilled in the art aware of said document.

As a result, the subject matter of claims 17 to 21 does not involve an inventive step (PCT Article 33(3)).

Box No. V — Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3.2 Claims 28-33:

The features disclosed in claims 28-30 are conventional in the production of such tablets. What is more, the properties mentioned in claims 32 and 33, whether they be mechanical (low friability, for example, < 1%) or relate to dissolution kinetics (high disintegration rate, for example, < 60 seconds), are desirable criteria in this field and a person skilled in the art knows how to arrive at such desired properties by adding specific additives to the granules in the mixture (see for example, D3, page 8, lines 19-26; page 12, lines 12-17; page 13, lines 10-18; and page 16, lines 18-30).

It follows that the subject matter of claims 28 to 33 does not involve an inventive step (PCT Article 33(3)).